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CHANGES IN CARDIAC OUTPUT FOLLOWING THE ADMINISTRATION OF SARIN AND OTHER PHARMACOLOGICAL AGENTS.

PART 2

Correlation of Ballistocardiographic and direct flow measurements in the dog, and observations on the effects of Sarin.

BY

R.J. SHEPHARD

PORTON TECHNICAL PAPER No. 735

C.D.E.E.
Porton
Wilts.

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DATE 13th June, 1960

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SUMMARY

1. Ballistocardiograph (B.C.G.) estimates of cardiac output in the dog have been compared with direct measurements of aortic flow made by venturi tube cannula.

2. The relationship between indirect and direct flow measurements was not linear, but the B.C.G. gave a correct qualitative index of flow changes produced by Sarin, pressor amines, and haemorrhage following [illegible] inhalation the B.C.G. indicated a small increase of cardiac output not shown by the aortic flow-meter.

3. Little improvement in the accuracy of the B.C.G. can be expected from modifications of table design, since the errors arise mainly from the action of the drugs tested on aortic cross section, peripheral vascular tone, rate of cardiac ejection, and overlap of successive ballistic waves.

4. Sarin had no effect on the cardiovascular system of the dog at a dose of 5 µg/kg.

A dose of 20 µg/kg gave slowing of the pulse and a fall of blood pressure, but an increase of stroke volume, after a lag period of 20 - 180 sec. These changes were reversed by 1.2 mg of atropine (with continued artificial respiration), but in some cases the blood pressure later again fell. This secondary effect was reversed by pressor amines.

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INTRODUCTION

Although the ballistocardiograph (B.C.G.) gives some indication of cardiac output, it is necessary also to use more direct methods of flow measurement to validate the changes observed in a given test situation. For reasons discussed in the previous paper, direct measurements of cardiac output were not possible in our experimental subjects. The necessary calibration was therefore carried out on the dog, using a scaled-down B.C.G. These experiments are now reported.

Direct measurements of aortic flow and cardiac output calculated from the B.C.G. have been compared during the administration of Sarin (isopropyl methyl phosphonofluoridate), and also following a number of procedures giving large changes of blood pressure, since it has been suggested that the B.C.G. is particularly liable to error where the blood pressure varies widely (1).

Much larger doses of Sarin could be given to the dogs than would be possible in human experiments. Previous authors have found a considerable decrease of cardiac output following large doses of cholinesterase inhibitors (2, 3), and it has been suggested (4, 5, 6) that in some species cardiac or peripheral vascular failure has been a factor in late deaths, despite treatment with atropine. This has considerable practical importance, for if a depression of cardiac output occurred in human subjects, this might point a need for pressor amines in the treatment of severe cholinesterase poisoning, as suggested by de Candole (4-6). Accordingly, consideration has been given to the effects of pressor amines, and their value is therapy.

METHODS

1. Preparation. Mongrel dogs of 10-15 kg/wt were anaesthetized with pentobarbitone sodium B.P. (1 ml/kg I.P. of solution 45 mg/ml in 10% alcohol).

Drugs were administered via a cannula in the proximal end of the external jugular vein, and a second cannula in the distal end served for the collection of blood samples. Intra-arterial pressures were recorded by a carotid cannula connected to a saline-filled capacitance manometer. A tracheal cannula permitted controlled respiration. The descending aorta was exposed through the fifth or sixth intercostal space, and after tying intercostal vessels, a stainless steel venturi tube was inserted into the aorta. The main disadvantage of this technique was the need for a full dose of heparin to prevent clotting within the cannula. This led to venous oozing, particularly within the thorax, and a consequent deterioration in the general condition of the animal despite intravenous infusion of "Dextran" (sterile non-pyrogenic solution, 10% w/v in 5% dextrose). The initial hypotension noted in some experiments did not invalidate the comparison of B.C.G. and direct flow records; indeed it probably made the comparison more searching. However, it could have been a factor increasing the apparent value of pressor amines in the therapy of Sarin poisoning.

When preparation of the animal was complete, it was transferred to a low-frequency critically damped B.C.G. table as described in the previous paper (1). Hot water bottles were applied between recordings to prevent a fall of body temperature.

2. Aortic flow measurement

(a) Technique. A stainless steel venturi tube flowmeter cannula was designed to general principles described by Ower (7), the inlet angle being 20° and the outlet 5° (Fig.1). The pressure tappings were initially made very small (14/10,000 in.) to avoid disturbing pressure/flow relationships in the primary axis of the tube, but problems arose from air locks and clotting of blood within the tappings. A second model with larger (1/16 in.) tappings overcame these difficulties, and still gave a water calibration curve corresponding closely with the theoretical* results for a venturi tube of these dimensions (Fig.1). The calibration curve for whole blood was rather different, presumably owing to the onset of turbulence within the constriction, but was still reproducible, and the differential pressure was of a suitable order for estimating aortic flow.

Differential pressures were measured by a pressurized U-tube; the upper ends of the two arms were connected via a three-way tap, and the amount of air in the system adjusted so that blood rose about half way up the two tubes.

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* Application of Bernouilli's theorem shows that in a perfect venturi system with no loss of pressure head:

$$\frac{P_1 - P_2}{d} = \frac{V_2^2 - V_1^2}{2g}$$

where P_1 and P_2 are the respective pressures and V_1 and V_2 the respective linear velocities before and after entering the constriction.

Flow was calculated from the mean differential pressure at any given time, using the blood calibration curve of Fig.1.

(b) Sources of error.

(i) Viscosity changes. Since flow is turbulent the differential pressure across the venturi is viscosity dependent. A gradual alteration of viscosity will result from the Dextran infusion, but this should not be sufficient to mask the relative changes produced by the different drugs. Alterations of haematocrit following Sarin administration are small and insufficient to account for the observed changes of differential pressure.

(ii) Phasic changes of flow. These were minimized by the air connecting the two limbs of the U-tube. As Ower (7) has pointed out, errors from pulsatile flow in a venturi are small if flow variations are kept below 25% of mean flow.

(iii) Redistribution of flow. The principle of calibration tacitly assumes that the venturi tube in the descending aorta receives a constant proportion of the total cardiac output. However, there is at present no reason to suppose that sarin produces a redistribution of flow between the upper and lower halves of the body.

3. B.C.G. cardiac output measurement. The simple empirical formula described in the previous paper of this series was used to calculate relative cardiac output:

$$\text{relative stroke volume} = \frac{\text{IJ amplitude x blood pressure factor}}{\text{IJ time}}$$

Values for cardiac output were computed using both the empirical blood pressure factor of Nickerson, and also the modified blood pressure factor derived from Roy's aortic pressure/volume curve.

RESULTS

1. Comparison of B.C.G. and aortic flow. Extensive comparisons of the B.C.G. cardiac output values with directly metered aortic flow rates were carried out in three dogs over a wide range of blood pressures from severe hypertension to terminal hypotension. Findings in the three animals were essentially similar, and to permit pooling of the data, flow values have been expressed as ml/kg/min.

When insertion of the aortic cannula and other surgical procedures had been completed, the dogs were in a state of moderate hypotension (mean systemic blood pressure 50-70 mm Hg). At this stage, the B.C.G. apparatus was so adjusted that the ratio of B.C.G. to direct flow reading was unity or a little less. Blood pressure was then increased by pressor amines, and finally reduced to very low values by prolonged bleeding. Qualitative agreement between the B.C.G. and direct flow readings was maintained throughout these experiments, but a quantitative relationship could not be demonstrated over more than a limited range of blood pressures (Fig.2, Table 1).

Assuming the descending aorta to receive one half of the total cardiac output, the observed absolute flow values conformed quite well with previous figures for dogs under barbiturate anaesthesia(8). With either method of calculation, the B.C.G. over-estimated the flow at high blood pressures, and under-estimated the flow at low pressures; expressing the calibration in terms of a ratio (Table 1), the Nickerson formula yielded a ten-fold change of slope,* and with the modified blood-pressure factor a four-fold change of slope still occurred over this range of blood pressures.

2. Effect of Sarin. B.C.G. readings were obtained from five dogs during the course of treatment with sarin and atropine. Results are summarized in Table 2, and detailed values for one experiment on dog 1 are plotted in Fig.4.

An intravenous dose of 5 µg/kg produced no consistent change of pulse rate, and although the B.C.G. did indicate a small decrease of cardiac output, this was not confirmed by direct flow measurements. The critical dose needed to produce cardiac slowing was of the order 20 µg/kg. In one dog (No.5), slowing was produced by 15 µg/kg, but only after a lag of 5 min. In three dogs, a dose of 20 µg/kg produced sudden and marked cardiac slowing from 20 - 180 sec after the injection. In the remaining animal (No.3) 20 µg/kg of sarin had little effect, but 2 min after injection of an additional 10 µg/kg the pulse became both slow and irregular. The lesser sensitivity of this animal to sarin cannot be attributed to the size of the blood cholinesterase pool (Table 2), and for the present it remains unexplained.

Slowing of the heart was associated with a fall of blood pressure (diastolic greater than systolic) and of calculated cardiac output, but stroke volume was normal or increased. The directly measured flow in the descending aorta also showed some decrease, but this was never as great as indicated by the B.C.G. (Figs. 3 and 4). In the experiment illustrated, both the long lag period prior to the response and the partial recovery of B.C.G. and direct flow measurements during succeeding minutes suggest that the total dose of sarin received (20 µg/kg) was only just sufficient to produce an effect on the heart. This is in striking contrast to the blood cholinesterase values, which remained 80% depressed. (Table 2).

An intravenous injection of 0.10 - 0.12 mg/kg atropine was sufficient to restore the pulse rate to the pre-sarin value in all dogs. In dog No.4 a smaller dose (0.06 mg/kg) was given, but when the pulse rate continued to deteriorate, a second injection was given. In the experiment illustrated in Fig.4, the effect of atropine was apparent within 10 seconds but in other dogs showing an earlier and more marked showing of the pulse with sarin, the same dose of atropine sometimes took 30 seconds to produce a response. In all cases, the increase of pulse rate occurred quite suddenly. Immediately, both systolic and diastolic pressures were elevated above previous resting values, and both the B.C.G. and the aortic cannula measurements indicated a rise of cardiac output. However, the alteration in cardiac output indicated by the B.C.G. was much distorted by the associated changes of blood pressure. In the experiments of Fig.4, the blood pressure correction factor was sufficiently large to convert a decrease of B.C.G. amplitude to an increase of calculated cardiac output. Obviously in such circumstances, the B.C.G. cannot have more than qualitative significance.

The small secondary fall of blood pressure seen in the minutes following atropine injection (Fig.4) may in this experiment indicate no more than relief of tissue hypoxia developed during the period of cardiac slowing. In other dogs (particularly No.3 and No.5), the later deterioration of blood pressure and cardiac output was marked. Intravenous administration of aramine (laevo-1(m-hydroxy phenyl) 2 amino 1-propanol hydrogen-d-tartrate) at this stage gave a very dramatic if brief restoration of both blood pressure and cardiac output (Figs. 3 and 5).

3. Effect of amyl nitrite. A crushed capsule of amyl nitrite (5 minims) was held over the inlet part of the Palmer respiration pump. A rapid fall of both systolic and diastolic pressure was observed (Fig.6), but there was little evidence of the compensatory tachycardia seen in man (9) either because the pressor reflexes had been depressed by anaesthesia, or because the initial hypotension was already giving maximal stimulation of the reflexes concerned. The B.C.G. showed a large increase in the amplitude of the IJ waves, but little change of cardiac output (a small increase of stroke volume <25%, developing over the course of the first minute). Again, a large pressure correction factor was involved in the calculation, and the result was shown to be in error by direct flow measurements which indicated no change of cardiac output apart from a fall of 3% in first minute.

4. Effect of pressor amines. An injection of 0.5 mg of adrenaline tartrate gave a dramatic but transient rise of both systolic and diastolic pressures, with an increase of pulse rate (Fig.7). Both B.C.G. and aortic cannula showed an increase of cardiac output, although owing to the large change of "Bloodpressure" factor, the B.C.G. much exaggerated the magnitude of change. Ephedrine sulphate (10 mg) produced a smaller but more sustained rise of blood pressure, and a larger increase of pulse rate. Both B.C.G. and cannula showed a sustained increase of cardiac output, but again the magnitude of change was exaggerated by the B.C.G.

In other dogs, aramine bitartrate was administered in 10 mg doses. The rise of blood pressure was as large as with adrenaline, but was more persistent. Both the B.C.G. and aortic cannula measurements showed an increase of flow, but again the B.C.G. much exaggerated the change.

5. Controlled haemorrhage. After administration of pressor amines, most experiments were terminated by deliberate bleeding from the external jugular vein. This gave a progressive fall of blood pressure (Fig.7), and terminally a fall of pulse rate. Both the B.C.G. and the aortic cannula indicated a progressive reduction of cardiac output.

DISCUSSION

1. Validity of B.C.G. technique. The present observations have shown that in a wide variety of experimental situations: after administration of sarin, adrenaline, ephedrine, or aramine, and during controlled haemorrhage, the B.C.G. gave a correct qualitative indication of changes in cardiac output.

Only with amyl nitrite did it indicate a small increase of flow where in fact no change occurred.

The calibration curve against directly measured aortic flow-rates was non-linear, and in some cases changes of flow were grossly exaggerated. This is not surprising since the agents tested modify aortic cross-section, peripheral vascular tone, the rate of cardiac ejection, and pulse rate and hence overlap of successive ballistic waves; indeed, it is remarkable that the B.C.G. is so successful as a qualitative indicator of cardiac output. These factors, together with other sources of error such as variations in cardiac axis and heart/body coupling are largely outside the control of the investigator, and are unlikely to be overcome by any further improvements in table design. The results show that quantitative observations especially on man should be confirmed by direct flow measurements in an experimental animal, particularly where large changes of systemic blood pressure are involved.

The B.C.G. is useful, however, in showing the absence of change. Since sarin produced no measurable effect on any cardiac parameter in the dog at doses known to be safe in man, the B.C.G. may thus be considered an adequate tool to investigate the effects of this agent on the human heart, at these doses.

2. The effect of larger doses of sarin. Genuine effects upon the cardiovascular system were noted when the dose of sarin was increased from 5 to 20 µg/kg. The latter dose approximates the lower of two estimates of intravenous LD50 for the dog (19 µg/kg - 29 µg/kg) and the observed depression of [illegible] was in keeping with dosage of this order.

Despite their poor clinical condition due to the prolonged general anaesthesia and inevitable loss of blood during preparation even this dose sometimes took as long as three minutes to produce cardiac slowing and a fall of cardiac output. Direct measurements of aortic flow showed that the fall of output was due simply to the cardiac slowing, and stroke volume might actually be increased - at least initially. Wilson (10) made similar observations in the isolated heart-lung preparation of the dog; large doses of GB almost halved the heart rate, but cardiac output decreased by only 7%. Askew (11) also found that in the isolated rat heart, perfusion with GB decreased the rate but not the amplitude of cardiac contractions.

A single injection of atropine (1.2 mg i.v.) rapidly restored a normal pulse rate. The immediate rise of blood pressure following atropine therapy has been considered an expression of central anoxia, previously masked by the falling cardiac output. The fall of blood pressure must inevitably embarass the cerebral circulation to some extent, but other factors such as a disturbance of ventilation/perfusion relationships within the lung probably also contribute to the central anoxia.

The secondary fall of blood pressure in some animals is similar to that previously described in other species (4-6). However, in the present instance it is not certain how far this was a pure effect of sarin, and it may have been a combined response to sarin intoxication, prolonged anaesthesia, and the major surgical procedures. Wilson (10) has previously pointed out that anaesthesia can very readily convert a pressor response to sarin to a depressor response.

If the secondary fall in blood pressure was a genuine effect of sarin, it must have been a "nicotinic" response, since the central and muscarine-like cardiac and peripheral cardiovascular actions would be adequately counteracted by atropine. Ganglion block has usually been blamed, although it is possible that in the conscious animal muscular paralysis, by diminishing venous return, may make a significant contribution to this late failure. As noted by de Candole (1-6), the immediate situation can be restored by the use of pressor amines such as Aramine. In addition to their action on the heart and arterioles, such agents have a major effect on venous tone, and this may be a factor in their apparent effectiveness in the treatment of "nerve-gas" casualties.

The lag in the action of both sarin and atropine cannot be explained in terms of circulation time from the external jugular vein to the pacemaker; it could indicate slow penetration from the blood-stream to the pacemaker, but is most probably caused by circulation of the agent as a "slug", insufficient of the material leaving the blood stream during the first few circuits to inhibit the cholinesterases in cardiac muscle.

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REFERENCES

1. Shephard, R.J. (1960). P.T.P. 734
2. Holmstedt, B. and Skoglund, C.R.(1953). Acta physiol. Scand. 29 Supp.106, 40
3. De Burgh Daly, M. (1957). J. Physiol. 139, 273.
4. De Candole, C.A. (1956). S.T.P. 86, (D.R.B., Canada).
5. De Candole, C.A. (1956). S.T.P. 93, (D.R.B., Canada).
6. De Candole, C.A. and Sunahara, F.A. (1959). D.R.M.L. Rep. 227-1
7. Ower, E. (1949). The measurement of air flow (3rd Ed.)
8. Handbook of circulation (1959). Ed. Altman, P.L. W.A.D.C. Tech.Rept. 59-593, Wright Air Development Center, Ohio, U.S.A.
9. Shephard, R.J. (1960). P.T.P. 736
10. Wilson, K.M. (1949). P.T.P. 152.
11. Askew, B.M. (1958). P.T.P. 643.

TABLE 1. Correlation of cardiac output calculated from B.C.G. record with direct measurements of flow in descending aorta. Pooled data from 3 dogs, showing mean ± S.E.

(a) Mean Systemic Blood pressure (mm/Hg)	(b) Number of Comparisons	(c) Direct flow reading (ml/kg/min)	(d) Nickerson B.C.G. Formula (ml/kg/min)	(e) Modified B.C.G. Formula	(f) Ratio of d/c	(g) Ratio of e/c
Moderate hypotension (50 - 70)	24	39.8 ± 1.1	33.9 ± 2.9	33.8 ± 2.7	0.84 ± 0.05	0.84 ± 0.05
Normal tension (70 -100)	20	55.5 ± 2.7	168.7 ± 3.4	159.9 ± 3.4	3.04 ± 0.23	2.92 ± 0.20
Hypertension (> 150)	5	46.7 ± 2.5	118.5 ± 49.3	99.3 ± 39.6	2.38 ± 0.83	2.00 ± 0.66
Severe hypertension (100 - 150)	21	37.5 ± 0.8	30.0 ± 1.6	35.5 ± 2.0	0.80 ± 0.03	0.94 ± 0.04
Very severe hypotension (30 - 40)	18	35.2 ± 0.8	22.2 ± 2.5	30.2 ± 3.5	0.63 ± 0.07	0.86 ± 0.10
Terminal hypotension (< 30)	11	28.3 ± 1.6	9.3 ± 1.6	19.3 ± 3.0	0.31 ± 0.05	0.67 ± 0.10

TABLE 2. Effects of Sarin and atropine upon Cardiac function in dogs

Experimental Conditions	Pulse rate (beats/min)	Nickerson B.C.G. formula (ml/kg/min)	Modified B.C.G. formula (ml/kg/min)	Directly measured aortic flow (ml/kg/min)	Circulating cholinesterase values					
					Red Cell		Plasma		Whole blood	
					Michel units	% depression	Michel units	% depression	Michel units	% depression
Control (animal 1)	142	30.0	31.1	36.1	87	0	158	0	124	0
Sarin, 5 µg/kg i.v.										
30 sec	142	28.6	29.6	39.5						
1 min	143	27.1	28.1	39.5						
5 min	140	26.8	32.0	36.1						
15 min	141	31.4	38.4	38.5	58	33	105	34	84	32
Sarin, to 20 µg/kg i.v.										
1 min	138	30.8	35.8	37.4						
2 min	133	27.7	33.0	36.1						
3 min	65	9.4	13.5	33.8						
5 min	66	15.8	18.9	38.5						
Atropine 0.12 mg/kg i.v.										
10 sec	154	44.9	44.9	42.9						
30 sec	153	27.9	27.9	42.9						
1 min	155	28.2	28.2	42.9						
5 min	152	22.0	24.8	38.5	19	78	17	89	20	84
Controls (animal 2)	198	17.2	24.2	31.0						
	204	12.5	21.9	31.0						
Sarin, 5 ug/kg i.v.										
1 min	192	12.3	21.5	28.0						
2 min	194	12.4	21.7	28.5						

Sarin to 20 µg/kg i.v.										
20 sec	118	2.9	7.0	28.0						
30 sec	28	–	–	–						
Atropine 0.12 mg/kg i.v.										
20 sec	177	–	–	–						
1 min	214	25.6	29.5	29.5						
2 min	200	–	–	–						
Control (animal 3)	163	28.5	27.6	–	68	0	123	0	97	0
Sarin, 5 µg/kg i.v.										
30 sec	162	24.2	23.4							
15 min	160	19.4	18.7	–	65	4	105	15	89	8
Sarin, to 20 µg/kg i.v.										
30 sec	160	19.2	18.3							
5 min	143	17.6	16.8							
15 min	144	11.5	10.8	–	11	84	26	79	22	77
Sarin, to 50 µg/kg i.v.										
30 sec	143	11.3	10.7							
1 min	142	10.0	9.4							
2 min	114 (irreg.)	5.2	5.0							
Atropine 0.10 mg/kg i.v.										
10 sec	94	3.5	3.3							
30 sec	131	9.6	9.2							
1 min	162	25.0	23.6							
5 min	140	7.3	6.9							

TABLE 2 (cont'd)

Control (animal 4)	118	34.7	57.8
	116	22.0	44.0
Sarin, 5 µg/kg i.v.			
30 sec	116	19.4	38.8
15 min	117	19.6	39.0
Sarin to 20 µg/kg i.v.			
30 sec	116	19.9	39.8
60 sec	91	21.2	42.4
70 sec	61	19.0	36.9
Atropine 0.06 mg/kg i.v.			
30 sec	12	1.7	5.1
Atropine to 0.12 mg/kg i.v.			
30 sec	101	138.8	183.0
60 sec	135	99.5	147.0
3 min	117	67.4	106.0
Control (animal 5)	160	42.6	40.1
Sarin 15 µg/kg i.v.			
30 sec	135	15.9	18.3
5 min	51	8.4	10.9
Atropine 0.12 mg/kg i.v.			
10 sec	53	4.4	5.2
20 sec	140	17.1	18.0
Atropine to 0.24 mg/kg i.v.			
30 sec	248	10.9	19.1

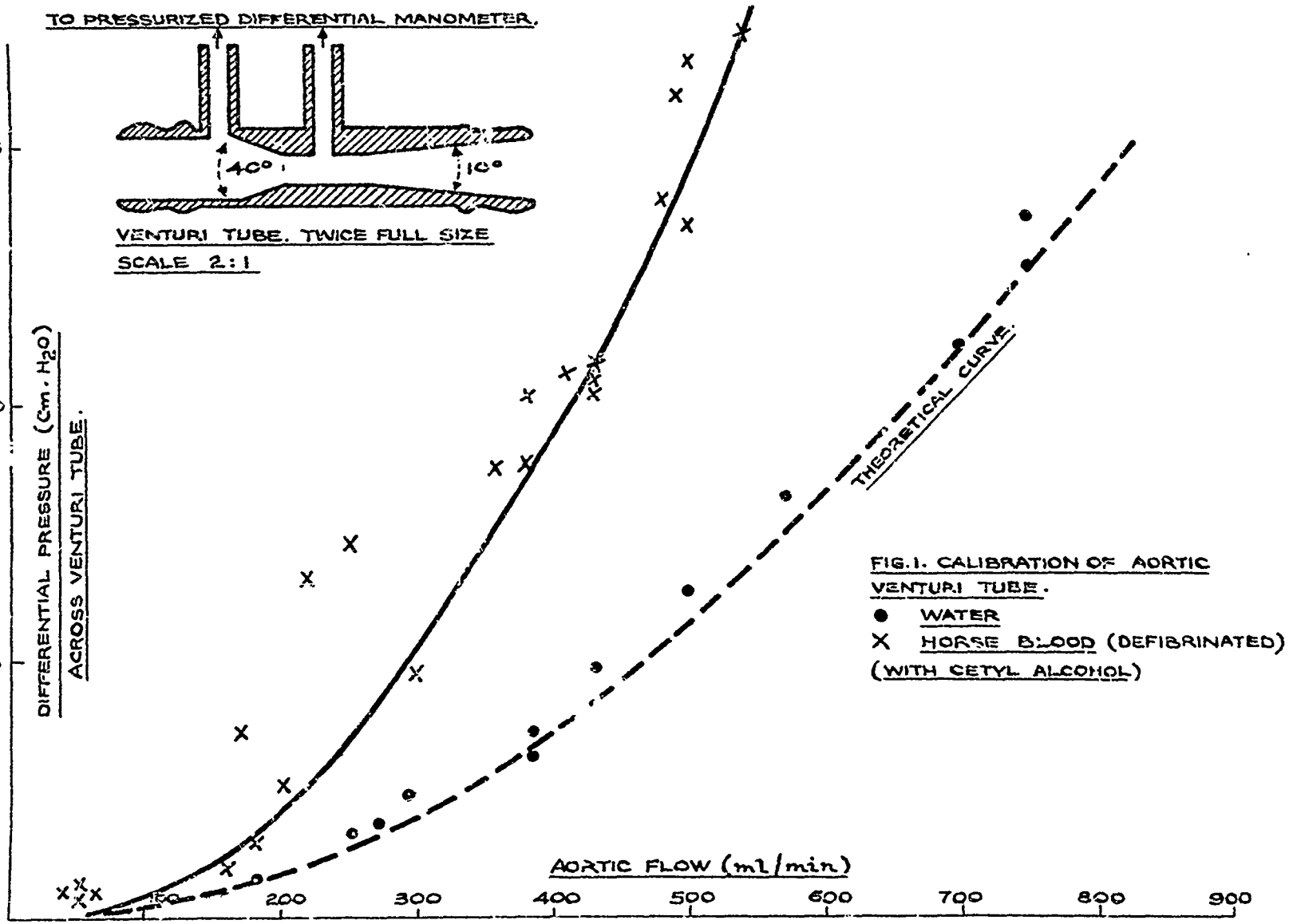

FIG. 1. CALIBRATION OF AORTIC VENTURI TUBE.

● WATER

X HORSE BLOOD (DEFIBRINATED) (WITH CETYL ALCOHOL)

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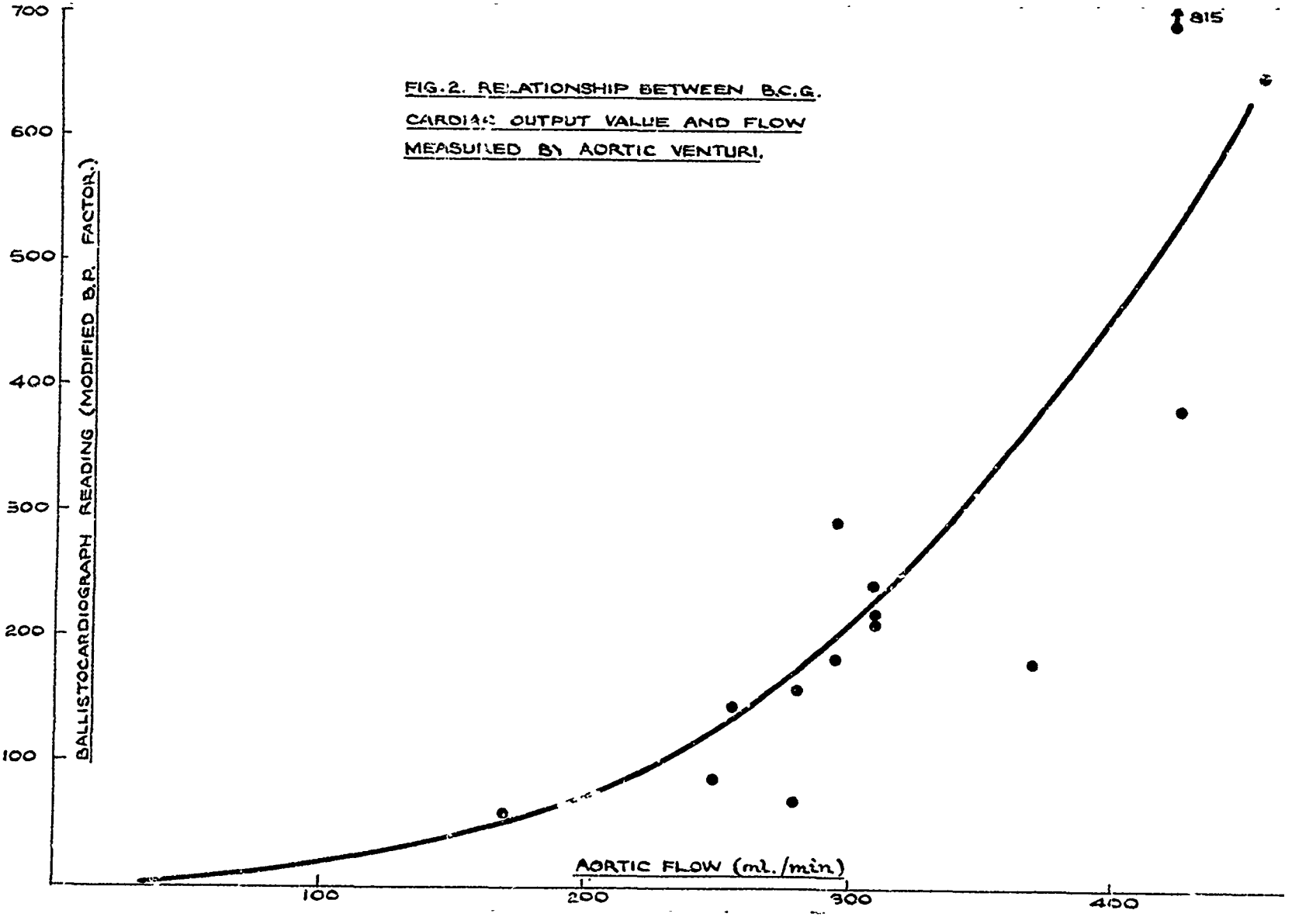
FIG. 2. RELATIONSHIP BETWEEN B.C.G. CARDIAC OUTPUT VALUE AND FLOW MEASURED BY AORTIC VENTURI.



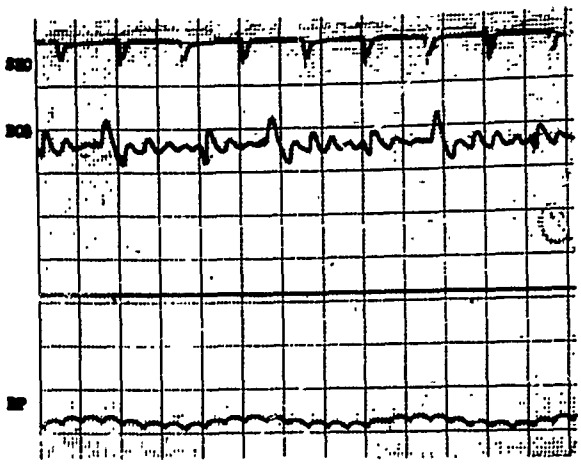


Fig. 3.1. Carotid blood pressure and E.C.G. record from dog anaesthetised with pentobarbitone Sodium.

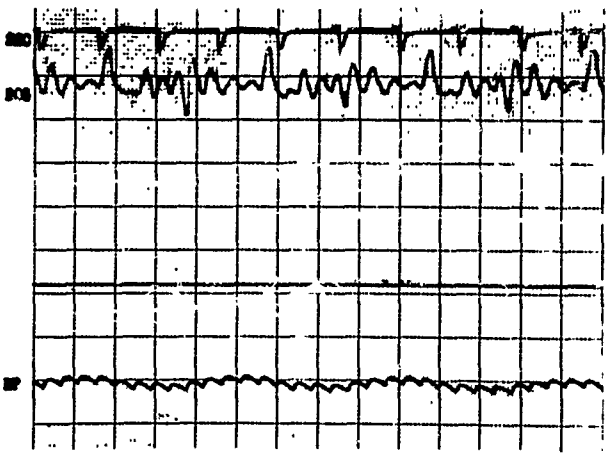


Fig. 3.2. Same dog, following intravenous injection of Sarin, 5 μg/kg.

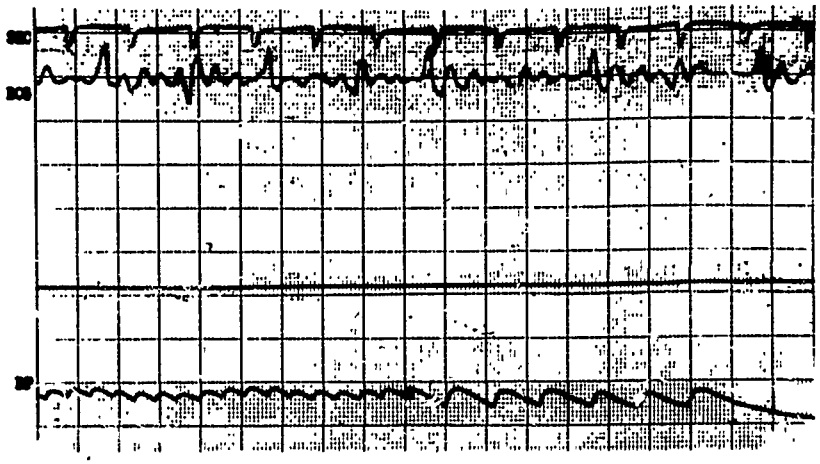


Fig. 3.3. Same dog, after injection of further 15 µg/kg. of Sarin. A sudden slowing of the pulse occurred 22 sec after injection.

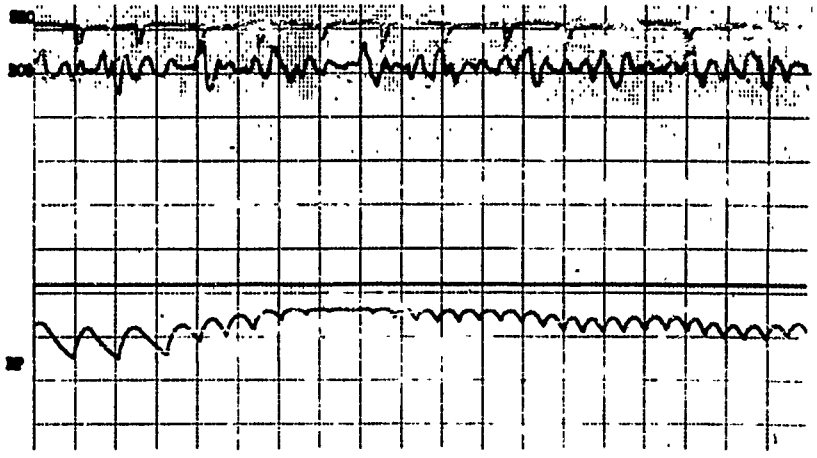


Fig. 3.4. Same dog after treatment with atropine (0.12 mg/kg I.v.). The pulse rate is restored suddenly to the Control level 14 sec after treatment.

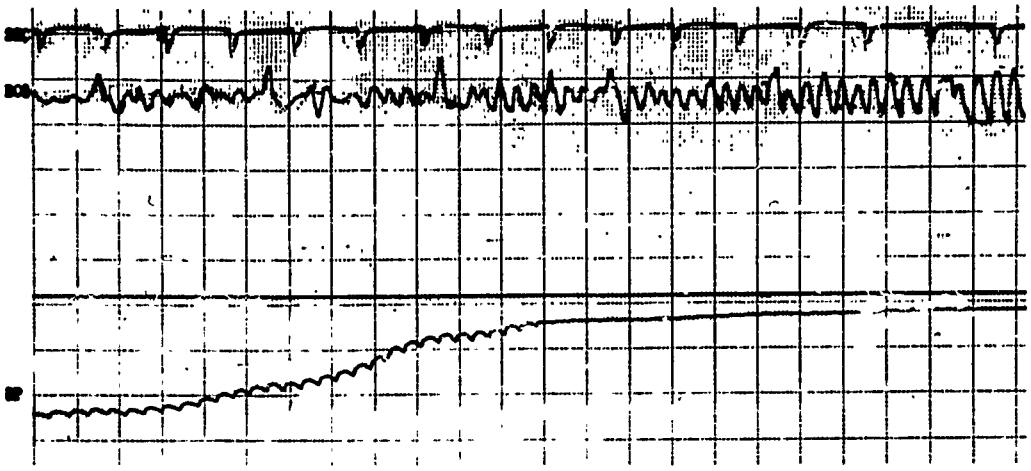


Fig. 3.5. Same dog 5 min after atropine injection. Cardiac output and systemic blood pressure showed a secondary deterioration, but were restored by injection of Aramine (0.5 mg/kg I.V.).

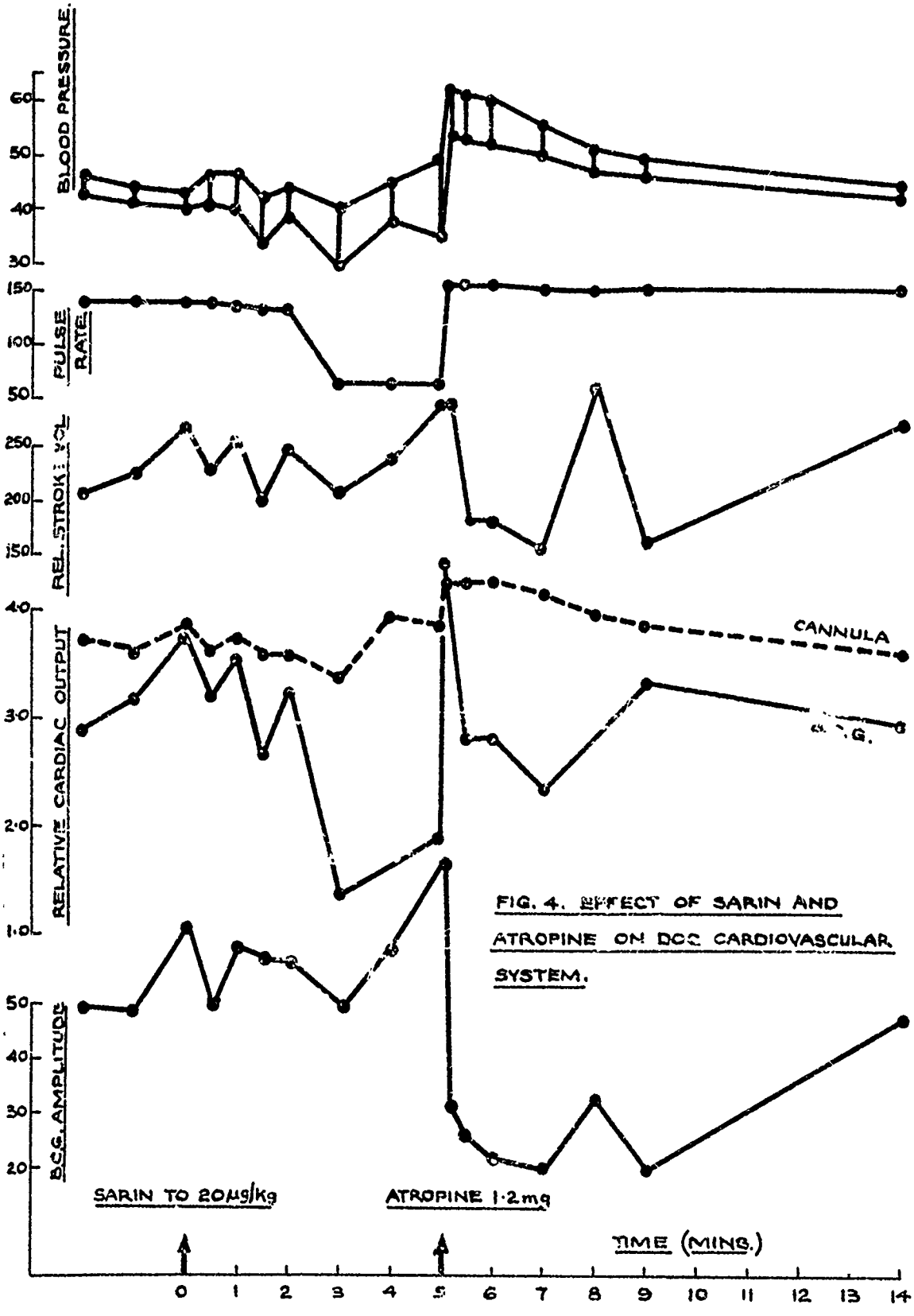
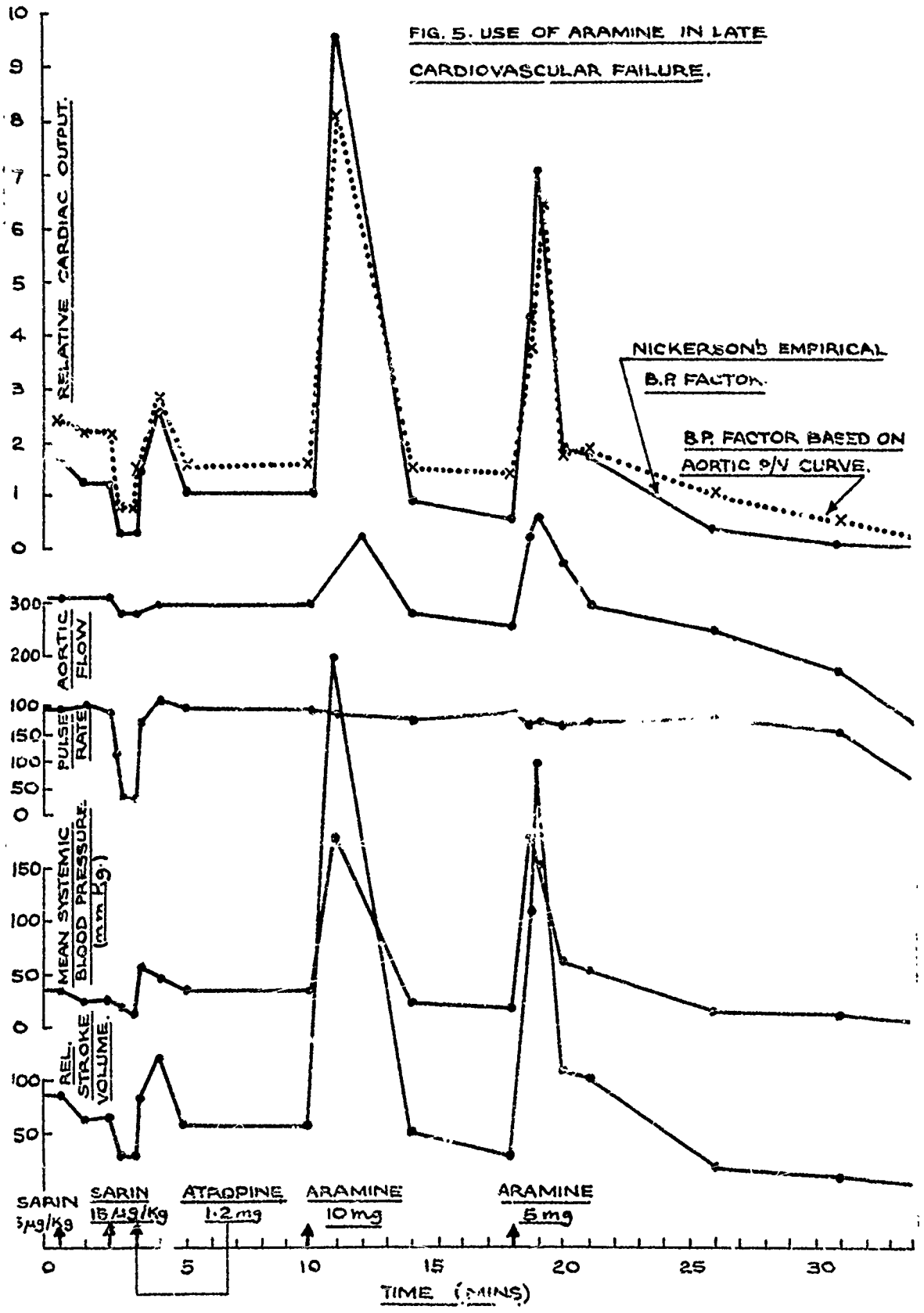


FIG. 4. EFFECT OF SARIN AND ATROPINE ON DOG CARDIOVASCULAR SYSTEM.



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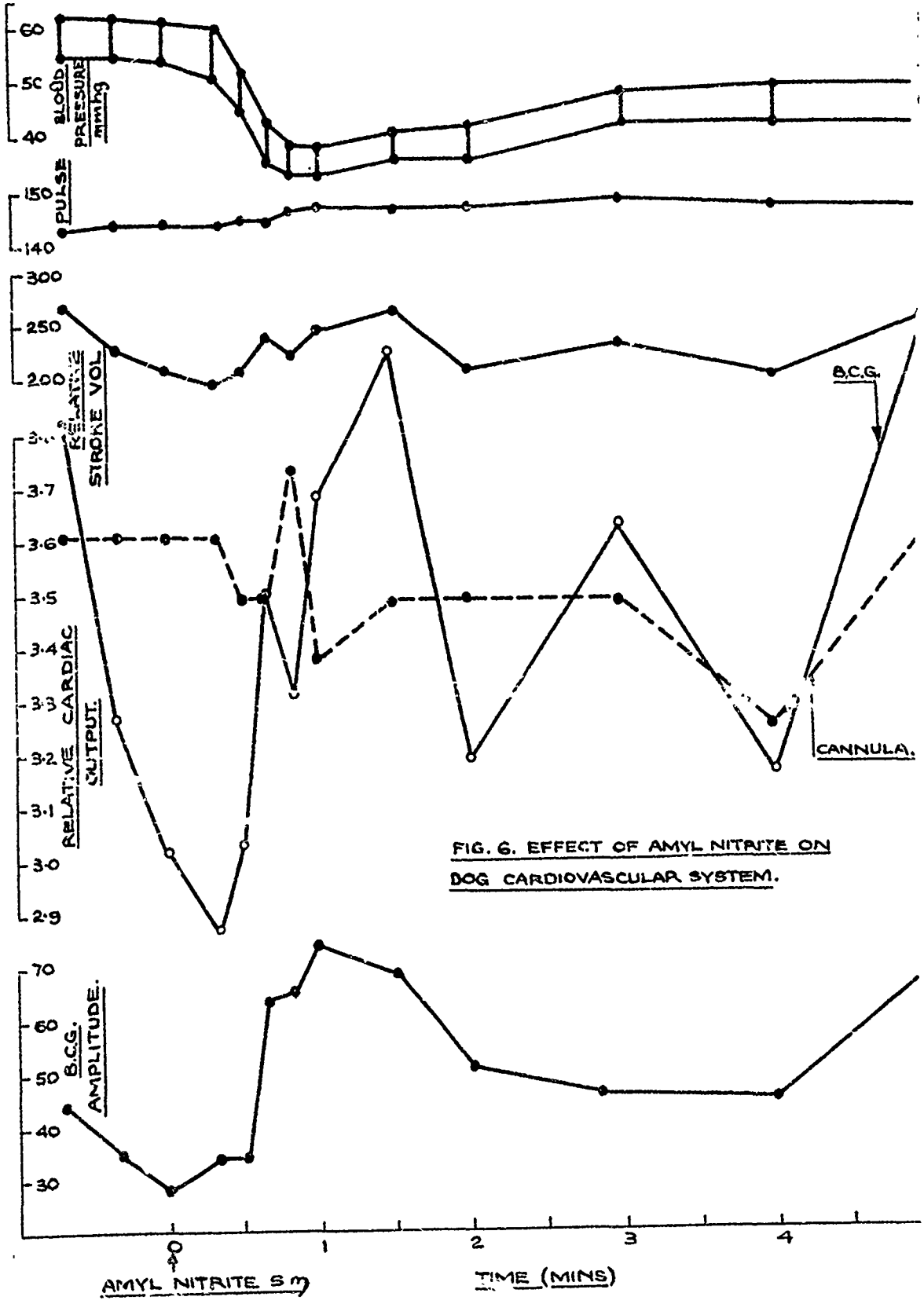
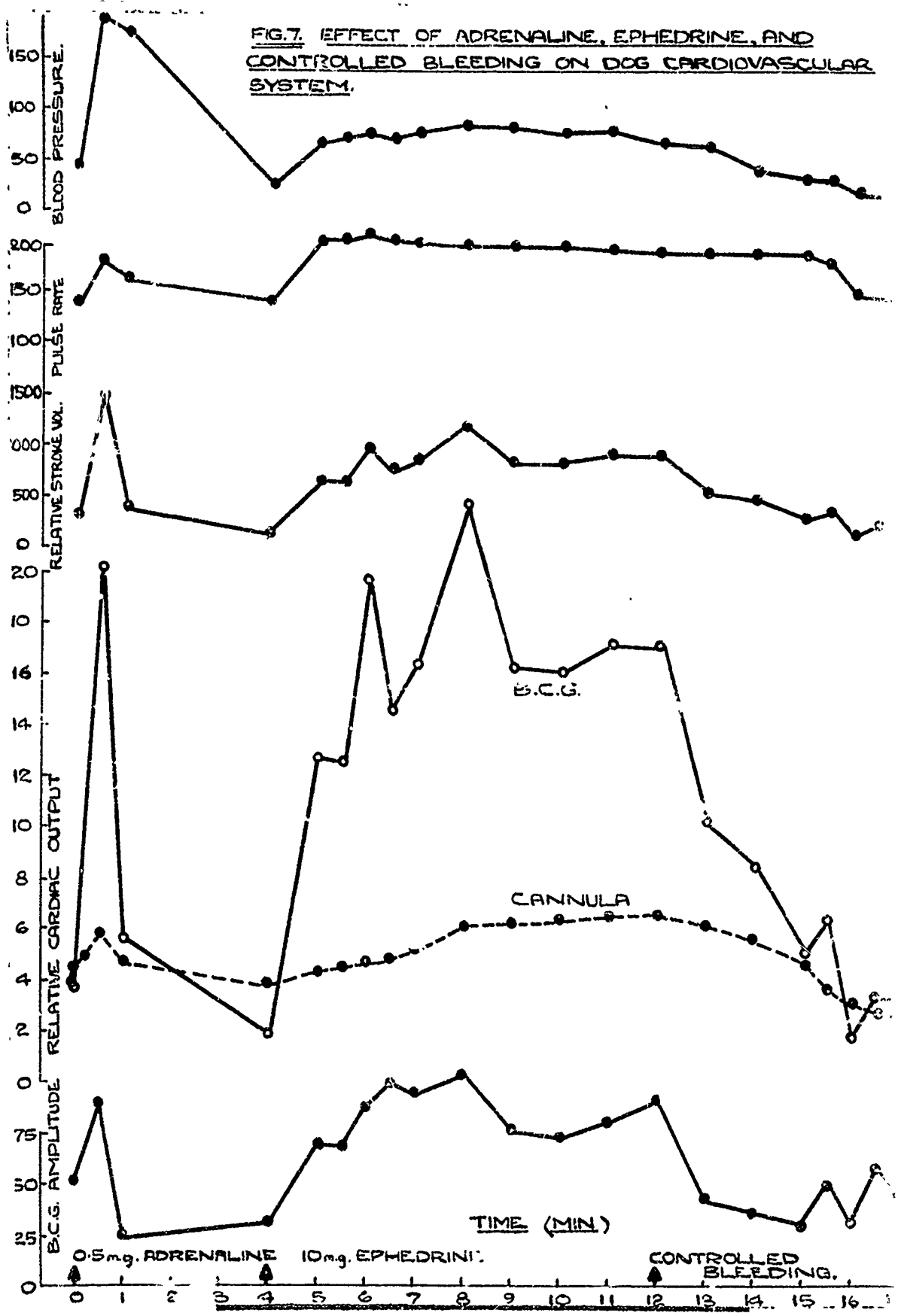


FIG. 6. EFFECT OF AMYL NITRITE ON DOG CARDIOVASCULAR SYSTEM.

FIG.7. EFFECT OF ADRENALINE, EPHEDRINE, AND CONTROLLED BLEEDING ON DOG CARDIOVASCULAR SYSTEM.



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